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L1	mageko	5	L1

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L1 0 MAGEKO

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L2 187730 TRANSGEN? OR KNOCKOUT

=> s l2 (3a)(mouse or mice)
L3 99284 L2 (3A)(MOUSE OR MICE)

=> s l1 or knock-in or knockin or knock in
L4 12923 L1 OR KNOCK-IN OR KNOCKIN OR KNOCK IN

=> s l2 or l4
L5 197392 L2 OR L4

=> s l5 (3a) (mouse or mice)
L6 102656 L5 (3A) (MOUSE OR MICE)

=> s l6 and VP16 and tetracycline repressor and GFP and VDE and neo
L7 0 L6 AND VP16 AND TETRACYCLINE REPRESSOR AND GFP AND VDE AND NEO

=> s l6 and VP16 and tetracycline repressor and GFP and VDE
L8 0 L6 AND VP16 AND TETRACYCLINE REPRESSOR AND GFP AND VDE

=> s l6 and VP16 and tetracycline repressor and GFP
L9 0 L6 AND VP16 AND TETRACYCLINE REPRESSOR AND GFP

=> s l6 and VP16 and tetracycline repressor
L10 9 L6 AND VP16 AND TETRACYCLINE REPRESSOR

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11 5 DUP REM L10 (4 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L11 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:311638 BIOSIS
DN PREV200100311638
TI C/EBPepsilon mediates myeloid differentiation and is regulated by the CCAAT displacement protein (CDP/cut) in 32Dcl3 cells.
AU Khanna-Gupta, Arati (1); Zibello, Theresa (1); Lekstrom-Himes, Julie; Berliner, Nancy (1)
CS (1) Internal Medicine/Hematology, Yale University School of Medicine, New Haven, CT USA
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 282a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB The role of C/EBPepsilon has been confirmed in ***knockout*** ***mice*** , which develop normally but fail to produce functional neutrophils. These mice die of opportunistic infections at 3-5 months of age. Neutrophils from C/EBPepsilon -/- mice have morphological and biochemical features similar to patients with neutrophil-specific secondary granule deficiency (SGD), a congenital disorder characterized by frequent bacterial infections and neutrophils that lack secondary granule proteins (SGP). Analysis of one SGD patient revealed a 5-basepair deletion in the C/EBPepsilon gene, resulting in an inactive truncated protein. Lack of functional C/EBPepsilon is postulated to cause this patient's disease. We previously demonstrated that overexpression of the transcriptional repressor CCAAT displacement protein (CDP/cut) in 32Dc13 cells suppresses SGP gene expression. This phenotype resembles that of C/EBP-/- mice and SGD patients. We therefore hypothesized that C/EBPepsilon was regulated by CDP/cut. We expressed wild type and mutant SGD C/EBPepsilon genes in 32Dcl3/Tet cells, which constitutively express a ***Tetracycline*** ***repressor*** (TetR)- ***VP16*** fusion protein. Stable transfection of 32D/Tet cells with a C/EBPepsilon cDNA cloned downstream of three TetR binding elements results in inducible C/EBPepsilon expression upon removal of Tet from the medium. Wild type but not mutant C/EBPepsilon expression in the 32D/Tet cells resulted in granulocytic morphology and lactoferrin (LF) gene expression. These data indicate that inducible C/EBPepsilon in 32D/Tet cells can drive granulocytic maturation.

Since SGP gene expression is dependent on C/EBPepsilon, and that expression is abrogated in 32Dcl3 CDP/cut overexpressing cells, we hypothesized that lack of SGP gene expression may reflect altered levels of C/EBPepsilon. Northern blot analysis of G-CSF-induced CDP/cut overexpressing 32Dcl3 cells revealed absence of C/EBPepsilon mRNA. Levels of C/EBPalpha transcript were unaffected. We conclude that repression of SGP gene expression in 32Dcl3/CDP/cut cells is mediated in two ways. The first is a direct interaction of CDP/cut with the promoters of the SGP genes, an observation we previously validated with the LF promoter. The second is an interaction between CDP/cut and C/EBPepsilon. We have isolated the C/EBPepsilon promoter and have identified a putative CDP/cut binding site. We have evidence for a role of this site in C/EBPepsilon expression and hence in SGP expression during neutrophil maturation.

L11 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 1996:746323 CAPLUS
DN 126:15526
TI Glucose-responsive, insulin-producing transgenic pancreatic .beta.-cells with proliferation regulated by tetracycline
IN Efrat, Shimon
PA Albert Einstein College of Medicine of Yeshiva University, USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9631242	A1	19961010	WO 1996-US4792	19960403
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2217652	AA	19961010	CA 1996-2217652	19960403
AU 9655375	A1	19961023	AU 1996-55375	19960403
AU 720662	B2	20000608		
EP 822834	A1	19980211	EP 1996-912616	19960403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11505411	T2	19990521	JP 1996-530530	19960403
US 6114599	A	20000905	US 1998-44297	19980319
US 6242254	B1	20010605	US 2000-492905	20000127
PRAI US 1995-418416	A	19950407		
WO 1996-US4792	W	19960403		
US 1998-44297	A1	19980319		

AB Glucose-regulated insulin producing pancreatic .beta.-cells whose proliferation is controlled by tetracyclines are described for use in the treatment of diabetes. Proliferation is controlled by a fusion protein of the ***tetracycline*** ***repressor*** tetR and ***VP16*** to regulate expression of an SV40 T antigen gene under control of a tet operator. The gene for the fusion protein is under control an insulin-responsive promoter. An animal carrying both constructs is prepd. by crossing animals transformed with one of the constructs and .beta.-cells carrying the both constructs are selected in vitro. The construction of these cells in mice is demonstrated.

L11 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 1997:51843 CAPLUS
DN 126:100260
TI Fusion proteins of the ***tetracycline*** ***repressor*** for use in tetracycline regulation of gene expression in eukaryotes
IN Bujard, Hermann; Gossen, Manfred; Hillen, Wolfgang; Helbl, Vera; Schnappinger, Dirk
PA BASF A.-G., Germany; Knoll Aktiengesellschaft
SO U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 383,754.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 12

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5589362	A	19961231	US 1995-485971	19950607
US 5464758	A	19951107	US 1993-76726	19930614
US 5650298	A	19970722	US 1994-260452	19940614
US 5654168	A	19970805	US 1994-275876	19940715
US 5789156	A	19980804	US 1995-383754	19950203
WO 9640892	A1	19961219	WO 1996-US9049	19960606
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI US 1993-76327	B2	19930614		
US 1993-76726	A2	19930614		
US 1994-260452	A2	19940614		
US 1994-270637	B2	19940701		
US 1994-275876	A2	19940715		
US 1995-383754	A2	19950203		
US 1995-485971	A	19950607		

AB Fusion proteins of amino acid-substituted tet repressors and transcription factors that bind class B tet operators that can be used in tetracycline regulation of expression of foreign genes in eukaryotes. Genes encoding these proteins are also described. The tet operators also have nucleotide substitutions in one or two of the 3'-bases (+4 or +6). A pool of multiply mutant tet repressor genes was generated by bisulfite mutagenesis of the tetR gene and mutants with a reverse regulation phenotype (induction of gene expression by tetracyclines rather than repression) were identified using a galK/lacZ/tet operator reporter system. Fusion proteins of the N-terminal regions of these proteins and herpes simplex ***VP16*** were prepd. by std. methods. Their efficacy was tested in a reporter gene system using the CMV promoter and a heptameric tet operator to regulate expression of a luciferase reporter in HR-5 cells. Doxycycline induced gene expression by 237-1660-fold and two genes under the control of tet operators could be induced coordinately. Fusion proteins of silencer domains, e.g. Krueppel or v-erbA proteins, are described for use as repressors. A combinatorial anal. of amino acid-substituted analogs of the repressor and base-substituted analogs of the operator was undertaken to find combinations showing the most effective induction or repression.

L11 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 1996:537416 BIOSIS
DN PREV199699259772
TI Temporal control of the Cre recombinase in ***transgenic*** ***mice*** by a tetracycline responsive promoter.
AU St-Onge, Luc; Furth, Priscilla A.; Gruss, Peter (1)
CS (1) Dep. Mol. Cell. Biol., Max-Planck-Inst. Biophys. Chem., Am Fassberg, 37018 Goettingen Germany
SO Nucleic Acids Research, (1996) Vol. 24, No. 19, pp. 3875-3877.
ISSN: 0305-1048.
DT Article
LA English
AB Gene-targeted mice derived from embryonic stem cells are a useful tool to study gene function during development. However, if the mutation is embryonic lethal and the gene is deleted from the onset of development, later functions in adult animals cannot be studied. Recently, the bacterial Cre-loxP site-specific recombination system has successfully been used in transgenic animals to produce tissue-specific and temporal deletions (Gu et al. (1993) Cell, 73, 1155-1164; Gu et al. (1994) Science, 265, 103-106; Kuhn et al. (1995) Science, 269, 1427-1429). We have evaluated the tetracycline responsive binary system (Gossen and Bujard (1992) Proc. Natl. Acad. Sci. USA, 89, 5547-5551) for its ability to transiently express the Cre recombinase in ***transgenic*** ***mice*** . In this system, a transactivator fusion protein composed of the ***tetracycline*** ***repressor*** (tetR) and the acidic domain of the herpes simplex viral protein 16 (***VP16***) can regulate the expression of the Cre gene from a promoter containing tet-operator (tetO) sequences. In the absence of tetracycline, the Cre gene is expressed and will induce site-specific recombination between two loxP sites. In the presence of tetracycline, the Cre gene will not be expressed and recombination will not occur.

L11 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1995:361280 BIOSIS
DN PREV199598375580
TI A modified tetracycline-regulated system provides autoregulatory, inducible gene expression in cultured cells and ***transgenic*** ***mice*** .
AU Shockett, Penny; Difilippantonio, Michael; Hellman, Nathan; Schatz, David G. (1)
CS (1) Howard Hughes Med. Inst., Yale Univ. Sch. Med., New Haven, CT 06510 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 14, pp. 6522-6526.
ISSN: 0027-8424.
DT Article
LA English
AB A system for tetracycline-regulated inducible gene expression was described recently which relies on constitutive expression of a tetracycline-controlled transactivator (tTA) fusion protein combining the ***tetracycline*** ***repressor*** and the transcriptional activation domain of ***VP16*** (Gossen, M. & Bujard, H. (1992) Proc. Natl. Acad. Sci. US.4 89, 5547-55511. This system yielded only low levels of transactivator protein, probably because tTA is toxic. To avoid this difficulty, we placed the tTA gene under the control of the inducible promoter to which tTA binds, making expression of tTA itself inducible and autoregulatory. When used to drive expression of the recombination activating genes 1 and 2 (RAG-1 and RAG-2), the autoregulatory system yielded both substantially higher levels of variable (diversity) joining (V(D)J) recombination activity (70-fold on average) and inducible expression in a much larger fraction of transfected cells (autoregulatory, 90%, vs. constitutive, 18%). In addition, this system allowed the creation of ***transgenic*** ***mice*** in which expression of a luciferase transgene was inducible tens to hundreds of times the basal levels in most tissues examined. Induced levels of expression were highest in thymus and lung and appear to be substantially higher than in previously reported inducible luciferase ***transgenic*** ***mice*** created with the constitutive system. With the modified system, inducible transactivator mRNA and protein were easily detected in cell lines by RNA and Western blotting, and transactivator mRNA was detected by RNA blotting in some tissues of ***transgenic*** ***mice*** . This autoregulatory system represents an improved strategy for tetracycline-regulated gene expression both in cultured cells and in transgenic animals.

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